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sulphonic, mandelic, salicylic, citric and other physiologically compatible acids, preferably in the presence of a suitable solvent permitting isolation of the salt.

5 The quaternary ammonium derivatives can be prepared by reacting the free base with an alkyl halide, preferably in the presence of an inert solvent.

10 On the other hand, when it is desired to convert the acid addition salt or the quaternary ammonium derivative to the free base, this can be accomplished by dissolving the salt in a suitable solvent, neutralizing the solution with a basic material, such as sodium hydroxide, and isolating the desired base by extraction or other suitable means.

According to a further feature of the present invention there are provided pharmaceutical compositions comprising as active ingredient at least one of the compounds having the general formula I and/or their physiologically compatible acid addition salts and quaternary ammonium derivatives, in admixture with suitable carriers and/or excipients.

25 Said pharmaceutical compositions may be solid (e.g. tablets, pills, coated pills, suppositories, capsules) or liquid (such as solutions, suspensions, emulsions, or injectable preparations). These preparations may be suitable for oral, rectal, or parenteral administration.

30 The carriers may be conventional organic or inorganic substances, such as starch, magnesium stearate, talc, stearine, water, polyalkylene glycols and magnesium carbonate.

35 The pharmaceutical compositions may contain additives such as emulsifying, stabilizing, disintegrating and wetting agents.

40 The preparations may comprise in addition to the compounds of the general formula I one or more other therapeutically active compounds.

The pharmaceutical compositions according to the present invention may be prepared by the usual methods of the pharmaceutical industry known *per se*, by admixing the active ingredient with suitable solid or liquid organic or inorganic pharmaceutical carriers and/or excipients and, if desired, with other therapeutically active compounds.

50 The new compounds according to the invention and their methods of preparation are further illustrated by the aid of the following Examples.

EXAMPLE 1

30 g. (0.2 moles) of 2-mercaptobenzimidazole and 24.4 g. (0.2 moles) of 2-(2-aminoethyl)-pyridine are heated at 150°C on a metal bath until the intensive evolution of ammonia gas ceases (about 3 hours).

After cooling, the product is dissolved in ethanol or acetone and the solution is decolourised with charcoal. The solution is then diluted with water, whereupon 2-(β -pyrid-2-ylethylthio)benzimidazole separates in crystalline form, with a yield of 80%.

If an analytical sample is crystallized from 50% ethanol, the pure base is obtained with a melting point of 75–77°C.

If gaseous hydrochloric acid is introduced into the acetone solution of the base so obtained, or the solution is acidified with a 1:1 mixture of ethanol and 38% HCl, then the white crystalline dihydrochloride of the amine separates, and has a melting point of 198–201°C.

If the acetone solution of the base, obtained as described above, is refluxed with methyl iodide, the yellowish white quaternary dimethyliodide salt separates, after cooling, and has a melting point of 246–248°C.

EXAMPLE 2

16.7 g. (0.1 moles) of 2-mercaptobenzothiazole are dissolved in 200 ml. of ethanol, whereafter 16.4 g. (0.1 moles) of 4-chloromethyl pyridine hydrochloride and 8 g. (0.2 moles) of NaOH dissolved in a small amount of water are added to the solution.

The reaction mixture is refluxed for two hours and sodium chloride (11 g.) is then separated by filtration. The filtrate is evaporated and the residue crystallized from aqueous acetone, to give solid 2-(pyrid-4-ylmethylthio)benzothiazole. Yield: 75%; m.p.: 85–87°C.

If the acetone solution of the base so obtained is acidified with hydrochloric acid, the yellowish-white dihydrochloride separates; m.p.: 174–177°C.

If the acetone solution of the base is refluxed with methyl iodide and is then diluted with ether, the quaternary monomethyliodide salt is precipitated in the form of yellow crystals having a melting point of 150–152°C.

The compounds listed in the following Table have been prepared by the methods described in Examples 1 and 2.

Ex. No.	R_1	R_2	Z	X	A	Y	n	Position of pyridine bond	According to Ex. No.	Yield %	M.p. $^{\circ}\text{C}$.	Empirical formula (mol. weight)	Analysis data	
													N %	S %
3	H	H	CH	NH	—	S	2	2	1	80	75—77	$\text{C}_{14}\text{H}_{13}\text{N}_3\text{S}$ (255.34)	16.46	12.55
4	H	H	N	NH	—	S	2	2	1	85	182—185	$\text{C}_{13}\text{H}_{12}\text{N}_3\text{S} \cdot 3\text{HCl}$ (365.73)	15.32	8.77
5	5— —CH ₃	6— —H	CH	NH	—	S	2	2	1 2	72 85	45—47	$\text{C}_{18}\text{H}_{16}\text{N}_3\text{S}$ (269.37)	15.60 15.54	11.91 11.89
6	5— —CH ₃	6— —CH ₃	CH	NH	—	S	2	2	1	90	67—68	$\text{C}_{18}\text{H}_{17}\text{N}_3\text{S}$ (283.40)	14.83	11.31
7	H	H	CH	NH	—	O	2	2	1	68	185—189	$\text{C}_{14}\text{H}_{13}\text{N}_3\text{O} \cdot 2\text{HCl}$ (312.21)	13.46	—

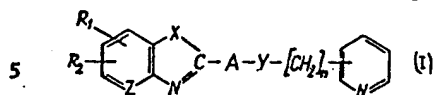
Ex. No.	R ₁	R ₂	Z	X	A	Y	n	Position of pyridine bond	According to Ex. No.	Yield %	M.p. °C.	Empirical formula (mol. weight)	Analysis data	
													N%	S %
8	H	CH	S	—	S	—	1	4	2	75	85—87	C ₁₃ H ₁₀ N ₃ S ₂	10.84	24.82
	H											(258.37)	10.27	25.18
9	H	CH	S	—	S	—	3	3	2	68	134—135	C ₁₃ H ₁₁ N ₃ S ₂ ·2HCl	7.79	17.85
	H											(359.36)	7.91	18.01
10	H	CH	O	—	S	—	1	4	2	72	169—173	C ₁₃ H ₁₀ N ₂ OS·2HCl	8.89	10.17
	H											(315.23)	9.29	9.62
11	H	CH	NH	—	S	—	1	4	2	90	128—129	C ₁₃ H ₁₁ N ₃ S	17.42	13.28
	H											(241.32)	16.96	13.77
12	H	CH	NH	—	S	—	3	3	2	95	104—106	C ₁₃ H ₁₁ N ₃ S·2HCl	12.28	9.36
	H											(342.31)	11.71	9.33
13	H	CH	NH	—	S	—	1	2	2	80	148—150	C ₁₃ H ₁₁ N ₃ S·2HCl	13.37	10.20
	H											(314.25)	12.92	10.42
14	5-Cl	CH	NH	—	S	—	1	2	2	65	172—174	C ₁₃ H ₁₀ ClN ₃ S·2HCl	12.05	9.20
	6-H											(348.70)	12.23	9.62

Ex. No.	R ₁	R ₂	Z	X	A	Y	n	Position of pyridine bond	According to Ex. No.	Yield %	M.p. °C.	Empirical formula (mol weight.)	Analysis data	
													N %	S %
15	H	N	NH	—	S	—	1	2	2	68	175—177	C ₁₁ H ₁₀ N ₄ S	23.12	13.23
	H											(242.31)	22.99	13.00
											191—194	C ₁₁ H ₁₀ N ₄ S·3HCl	15.93	9.12
												(351.70)	16.45	9.56
16	H	N	NH	—	S	—	1	4	2	69	162—165	C ₁₁ H ₁₀ N ₄ S·3HCl	15.93	9.12
	H											(351.70)	15.98	9.06
17	H	CH	NH	CH ₂	S	—	1	3	2	79	176—179	C ₁₁ H ₁₃ N ₃ S·2HCl	12.80	9.76
	H											(328.27)	12.35	10.03
18	H	CH	NH	—	S	—	1	3	2	93	182—185	C ₁₁ H ₁₁ N ₃ S·2HCl	13.37	10.20
	H											(314.25)	12.95	10.39
19	5—	CH	NH	—	S	—	1	2	2	82	120—121	C ₁₁ H ₁₁ N ₃ S	15.60	11.91
	—CH ₃											(269.37)	15.42	11.67
6—											198—200	C ₁₁ H ₁₁ N ₃ S·2HCl	12.28	9.36
	—CH ₃											(342.30)	12.26	9.73

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WHAT WE CLAIM IS:—

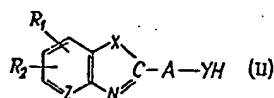
1. Compounds having the general formula I and acid addition salts and quaternary ammonium derivatives thereof,



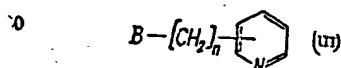
wherein

- A stands for an alkylene group containing 1—5 carbon atoms or a valence bond;
 X stands for a —NH group or an oxygen or sulphur atom;
 Y stands for a sulphur or oxygen atom;
 Z stands for a —CH— group or a nitrogen atom;
 R₁ stands for a hydrogen atom or a methyl group;
 R₂ stands for a hydrogen or chlorine atom or a —NO₂ or —CH₃ group; and
 n is an integer from 1 to 3.

2. A process for the preparation of compounds of general formula I and physiologically compatible acid addition salts and quaternary ammonium derivatives thereof, as claimed in claim 1, which comprises reacting an azole derivative having the general formula II



(wherein A, R₁, R₂, X, Y and Z are defined as in claim 1) with a pyridine derivative having the general formula III



wherein B stands for an —NH₂ group or a halogen atom and n is defined as in claim 1) or with a salt thereof, and, if desired, transforming the obtained product in a known way to a physiologically compatible acid addition salt or a quaternary ammonium derivative.

3. A process as claimed in claim 2, which comprises using 2 - (2 - amineoethyl) - pyridine as the pyridine derivative of general formula III.

4. A process as claimed in claim 2 or claim 3, in which the reaction is carried out at a temperature of 100 to 150° C.

5. A process as claimed in any of claims 2 to 4, in which the pyridine derivative of general formula III or its salt is reacted in an amount equivalent to that of the azole derivative of general formula II.

6. A process as claimed in any of claims 2 to 5, wherein the reaction is carried out in the presence of an acid-binding agent.

7. A process as claimed in claim 6, wherein sodium hydroxide is used as the acid-binding agent.

8. A process for the preparation of compounds of general formula I as defined in claim 1 substantially as herein described with reference to the Examples.

9. Compounds of the general formula I as defined in claim 1 whenever prepared by a process as claimed in any of claims 2 to 8.

10. Azole derivatives and acid addition salts and quaternary ammonium derivatives thereof as herein described in the Examples.

11. Pharmaceutical compositions comprising as active ingredient at least one compound of general formula I as claimed in claim 1, or a physiologically acceptable salt or quaternary ammonium derivative thereof, in admixture with one or more pharmaceutical carriers and/or excipients.

12. Pharmaceutical compositions as claimed in claim 11 in the form of tablets, pills, coated pills, suppositories, capsules, solutions, emulsions, suspensions or injectable preparations.

13. Pharmaceutical compositions as claimed in claim 11 or claim 12, containing at least one other therapeutically active compound in addition to the azole derivative of general formula I.

14. Pharmaceutical compositions according to any of claims 11 to 13, substantially as herein described.

15. A process for the preparation of pharmaceutical compositions as claimed in any of claims 11, 12 and 14, which comprises admixing at least one compound of general formula I, as claimed in claim 1 or physiologically compatible salt or quaternary ammonium derivative thereof with one or more pharmaceutical carriers and/or excipients.

16. A process as claimed in claim 15 wherein at least one other therapeutically active compound is added to the composition.

17. Pharmaceutical compositions as herein described, whenever prepared by a process as claimed in claim 15 or claim 16.

For the Applicants,
 FRANK B. DEHN & CO.,
 Chartered Patent Agents,
 Imperial House,

15/19, Kingsway, London, WC2B 6UZ.

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